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  1 ATGGCGCCAC CACCAGCTAG AGTACATCTA GGTGCGTTCC TGGCAGTGAC
    TACCGCGGTG GTGGTCGATC TCATGTAGAT CCACGCAAGG ACCGTCACTG
  1 MetAlaProP roProAlaAr gValHisLeu GlyAlaPheL euAlaValTh

 51 TCCGAATCCC GGGAGCGCAG CGAGTGGGAC AGAGGCAGCC GCGGCCACAC
    AGGCTTAGGG CCCTCGCGTC GCTCACCCTG TCTCCGTCGG CGCCGGTGTG
    rProAsnPro GlySerAlaA laSerGlyTh rGluAlaAla AlaAlaThrPro

101 CCAGCAAAGT GTGGGGCTCT TCCGCGGGGA GGATTGAACC ACGAGGCGGG
    GGTCGTTTCA CACCCCGAGA AGGCGCCCCT CCTAACTTGG TGCTCCGCCC
 35    SerLysVa lTrpGlySer SerAlaGlyA rgIleGluPr oArgGlyGly

151 GGCCGAGGAG CGCTCCCTAC CTCCATGGGA CAGCACGGAC CCAGTGCCCG
    CCGGCTCCTC GCGAGGGATG GAGGTACCCT GTCGTGCCTG GGTCACGGGC
    GlyArgGlyA laLeuProTh rSerMetGly GlnHisGlyP roSerAlaArg

201 GGCCCGGGCA GGGCGCGCCC CAGGACCCAG GCCGGCGCGG GAAGCCAGCC
    CCGGGCCCGT CCCGCGCGGG GTCCTGGGTC CGGCCGCGCC CTTCGGTCGG
 68  AlaArgAla GlyArgAlaP roGlyProAr gProAlaArg GluAlaSerP

251 CTCGGCTCCG GGTCCACAAG ACCTTCAAGT TTGTCGTCGT CGGGGTCCTG
    GAGCCGAGGC CCAGGTGTTC TGGAAGTTCA AACAGCAGCA GCCCCAGGAC
    roArgLeuAr gValHisLys ThrPheLysP heValValVa lGlyValLeu

301 CTGCAGGTCG TACCTAGCTC AGCTGCAACC ATGATCAATC AATTGGCACA
    GACGTCCAGC ATGGATCGAG TCGACGTTGG TAGTTTGAAG TACTAGTTAG
101 LeuGlnValV alProSerSe rAlaAlaThr IleLysLeuH isAspGlnSe

351 AATTGGCACA CAGCAATGGG AACATAGCCC TTTGGGAGAG TTGTGTCCAC
    TTAACCGTGT GTCGTTACCC TTGTATCGGG AAACCCTCTC AACACAGGTG
    rIleGlyThr GlnGlnTrpG luHisSerPr oLeuGlyGlu LeuCysProPro

401 CAGGATCTCA TAGATCAGAA CGTCCTGGAG CCTGTAACCG GTGCACAGAG
    GTCCTAGAGT ATCTAGTCTT GCAGGACCTC GGACATTGGC CACGTGTCTC
135    GlySerHi sArgSerGlu ArgProGlyA laCysAsnAr gCysThrGlu

451 GGTGTGGGTT ACACCAATGC TTCCAACAAT TTGTTTGCTT GCCTCCCATG
    CCACACCCAA TGTGGTTACG AAGGTTGTTA AACAAACGAA CGGAGGGTAC
    GlyValGlyT yrThrAsnAl aSerAsnAsn LeuPheAlaC ysLeuProCys

501 TACAGCTTGT AAATCAGATG AAGAAGAGAG AAGTCCCTGC ACCACGACCA
    ATGTCGAACA TTTAGTCTAC TTCTTCTCTC TTCAGGGACG TGGTGCTGGT
168  ThrAlaCys LysSerAspG luGluGluAr gSerProCys ThrThrThrA

551 GGAACACAGC ATGTCAGTGC AAACCAGGAA CTTTCCGGAA TGACAATTCT
    CCTTGTGTCG TACAGTCACG TTTGGTCCTT GAAAGGCCTT ACTGTTAAGA
    rgAsnThrAl aCysGlnCys LysProGlyT hrPheArgAs nAspAsnSer

601 GCTGAGATGT GCCGGAAGTG CAGCACAGGG TGCCCCAGAG GGATGGTCAA
    CGACTCTACA CGGCCTTCAC GTCGTGTCCC ACGGGGTCTC CCTACCAGTT
201 AlaGluMetC ysArgLysCy sSerThrGly CysProArgG lyMetValLy

651 GGTCAAGGAT TGTACGCCCT GGAGTGACAT CGAGTGTGTC CACAAAGAAT
    CCAGTTCCTA ACATGCGGGA CCTCACTGTA GCTCACACAG GTGTTTCTTA
    sValLysAsp CysThrProT rpSerAspIl eGluCysVal HisLysGluSer
```

FIG._1A

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 701 CAGGCAATGG ACATAATATA TGGGTGATTT TGGTTGTGAC TTTGGTTGTT
     GTCCGTTACC TGTATTATAT ACCCACTAAA ACCAACACTG AAACCAACAA
 235   GlyAsnGl yHisAsnIle TrpValIleL euValValTh rLeuValVal

 751 CCGTTGCTGT TGGTGGCTGT GCTGATTGTC TGTTGTTGCA TCGGCTCAGG
     GGCAACGACA ACCACCGACA CGACTAACAG ACAACAACGT AGCCGAGTCC
     ProLeuLeuL euValAlaVa lLeuIleVal CysCysCysI leGlySerGly

 801 TTGTGGAGGG GACCCCAAGT GCATGGACAG GGTGTGTTTC TGGCGCTTGG
     AACACCTCCC CTGGGGTTCA CGTACCTGTC CCACACAAAG ACCGCGAACC
 268  CysGlyGly AspProLysC ysMetAspAr gValCysPhe TrpArgLeuG

 851 GTCTCCTACG AGGGCCTGGG GCTGAGGACA ATGCTCACAA CGAGATTCTG
     CAGAGGATGC TCCCGGACCC CGACTCCTGT TACGAGTGTT GCTCTAAGAC
     lyLeuLeuAr gGlyProGly AlaGluAspA snAlaHisAs nGluIleLeu

 901 AGCAACGCAG ACTCGCTGTC CACTTTCGTC TCTGAGCAGC AAATGGAAAG
     TCGTTGCGTC TGAGCGACAG GTGAAAGCAG AGACTCGTCG TTTACCTTTC
 301 SerAsnAlaA spSerLeuSe rThrPheVal SerGluGlnG lnMetGluSe

 951 CCAGGAGCCG GCAGATTTGA CAGGTGTCAC TGTACAGTCC CCAGGGGAGG
     GGTCCTCGGC CGTCTAAACT GTCCACAGTG ACATGTCAGG GGTCCCCTCC
     rGlnGluPro AlaAspLeuT hrGlyValTh rValGlnSer ProGlyGluAla

1001 CACAGTGTCT GCTGGGACCG GCAGAAGCTG AAGGGTCTCA GAGGAGGAGG
     GTGTCACAGA CGACCCTGGC CGTCTTCGAC TTCCCAGAGT CTCCTCCTCC
 335   GlnCysLe uLeuGlyPro AlaGluAlaG luGlySerGl nArgArgArg

1051 CTGCTGGTTC CAGCAAATGG TGCTGACCCC ACTGAGACTC TGATGCTGTT
     GACGACCAAG GTCGTTTACC ACGACTGGGG TGACTCTGAG ACTACGACAA
     LeuLeuValP roAlaAsnGl yAlaAspPro ThrGluThrL euMetLeuPhe

1101 CTTTGACAAG TTTGCAAACA TCGTGCCCTT TGACTCCTGG GACCAGCTCA
     GAAACTGTTC AAACGTTTGT AGCACGGGAA ACTGAGGACC CTGGTCGAGT
 368   PheAspLys PheAlaAsnI leValProPh eAspSerTrp AspGlnLeuM

1151 TGAGGCAGCT GGACCTCACG AAAAATGAGA TCGATGTGGT CAGAGCTGGT
     ACTCCGTCGA CCTGGAGTGC TTTTTACTCT AGCTACACCA GTCTCGACCA
     etArgGlnLe uAspLeuThr LysAsnGluI leAspValVa lArgAlaGly

1201 ACAGCAGGCC CAGGGGATGC CTTGTATGCA ATGCTGATGA AATGGGTCAA
     TGTCGTCCGG GTCCCCTACG GAACATACGT TACGACTACT TTACCCAGTT
 401 ThrAlaGlyP roGlyAspAl aLeuTyrAla MetLeuMetL ysTrpValAs

1251 CAAAACTGGA CGGAACGCCT CGATCCACAC CCTGCTGGAT GCCTTGGAGA
     GTTTTGACCT GCCTTGCGGA GCTAGGTGTG GGACGACCTA CGGAACCTCT
     nLysThrGly ArgAsnAlaS erIleHisTh rLeuLeuAsp AlaLeuGluArg

1301 GGATGGAAGA GAGACATGCA AAAGAGAAGA TTCAGGACCT CTTGGTGGAC
     CCTACCTTCT CTCTGTACGT TTTCTCTTCT AAGTCCTGGA GAACCACCTG
 435   MetGluGl uArgHisAla LysGluLysI leGlnAspLe uLeuValAsp

1351 TCTGGAAAGT TCATCTACTT AGAAGATGGC ACAGGCTCTG CCGTGTCCTT
     AGACCTTTCA AGTAGATGAA TCTTCTACCG TGTCCGAGAC GGCACAGGAA
     SerGlyLysP heIleTyrLe uGluAspGly ThrGlySerA laValSerLeu

1401 GGAGTGA
     CCTCACT
 468 GluOP*
```

FIG._1B

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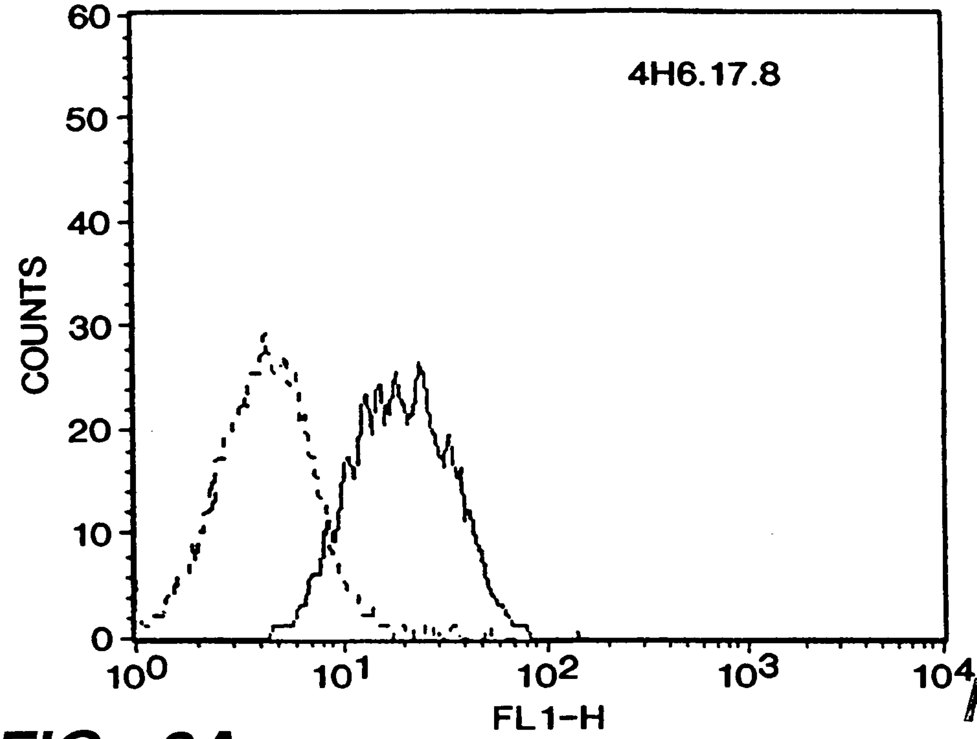

FIG._2A

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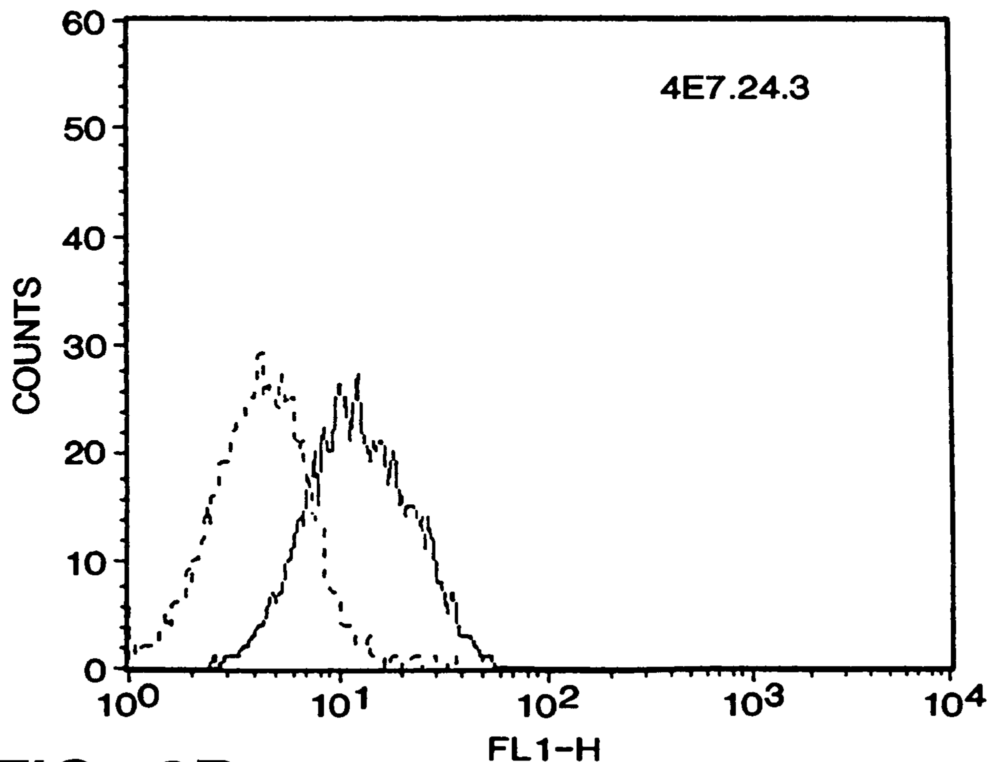

FIG._2B

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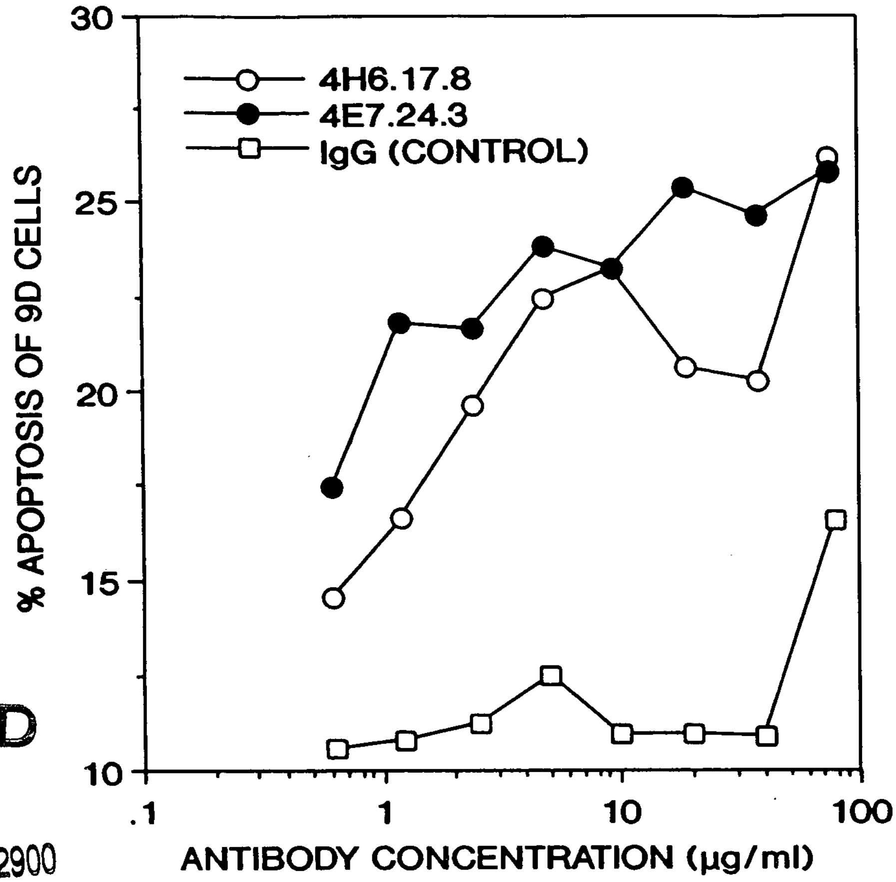

FIG._3

AFFINITIES OF Apo2Rs AND mAbs

		AFFINITY (pM)
DR4-IgG	to Apo2L	82
DR5-IgG	to Apo2L	1
mAb 4E7	to DR4-IgG	2
mAb 4H6	to DR4-IgG	5
mAb 5G11	to DR4-IgG	22
mAb 3F11	to DR5-IgG	20
mAb 3H3	to DR5-IgG	3

Affinities were determined using KinExA

FIG._7

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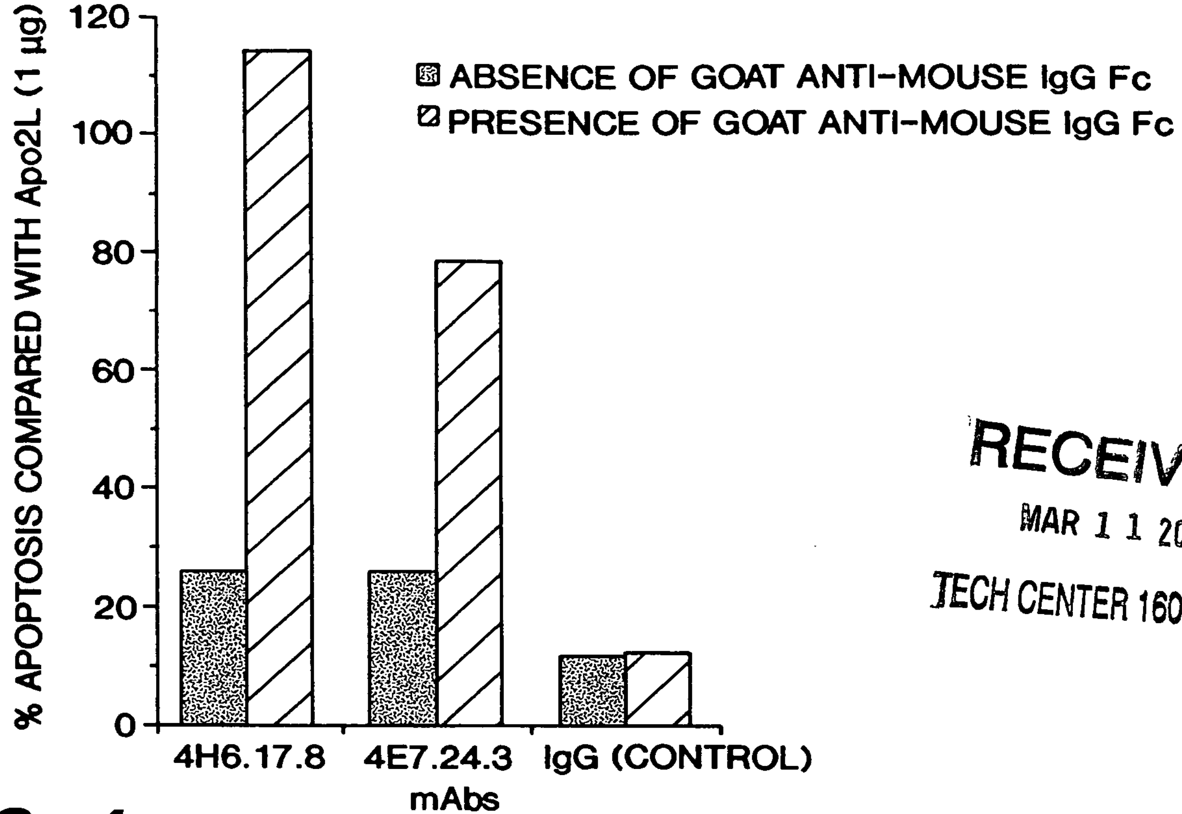

FIG._4

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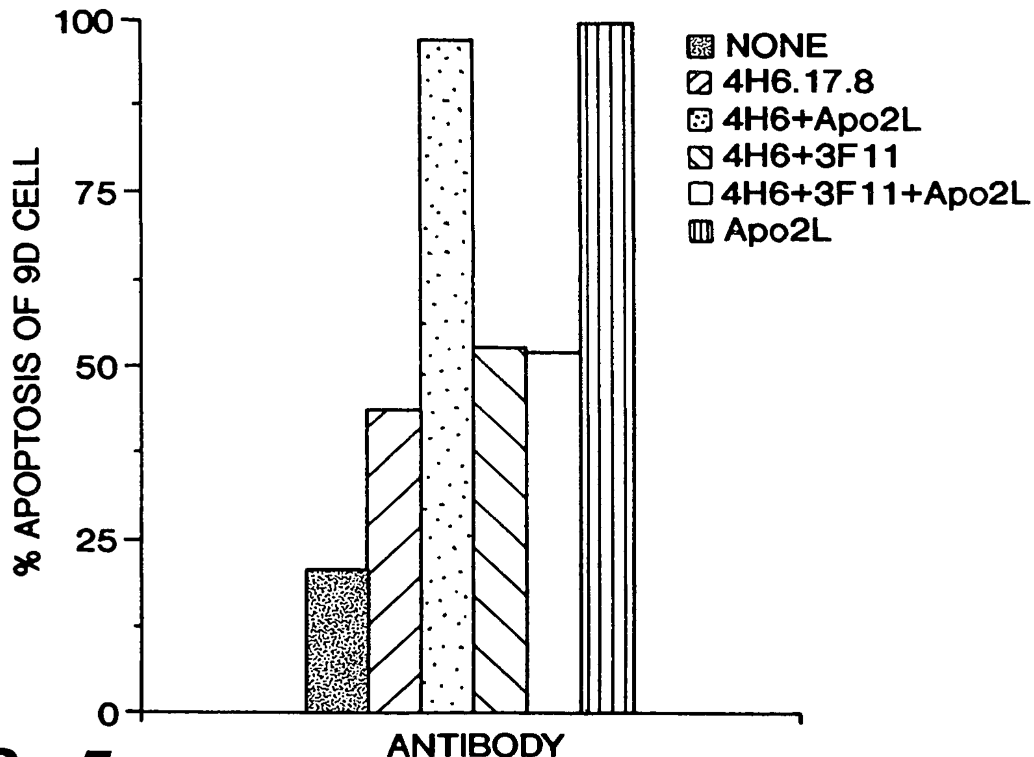

FIG._5

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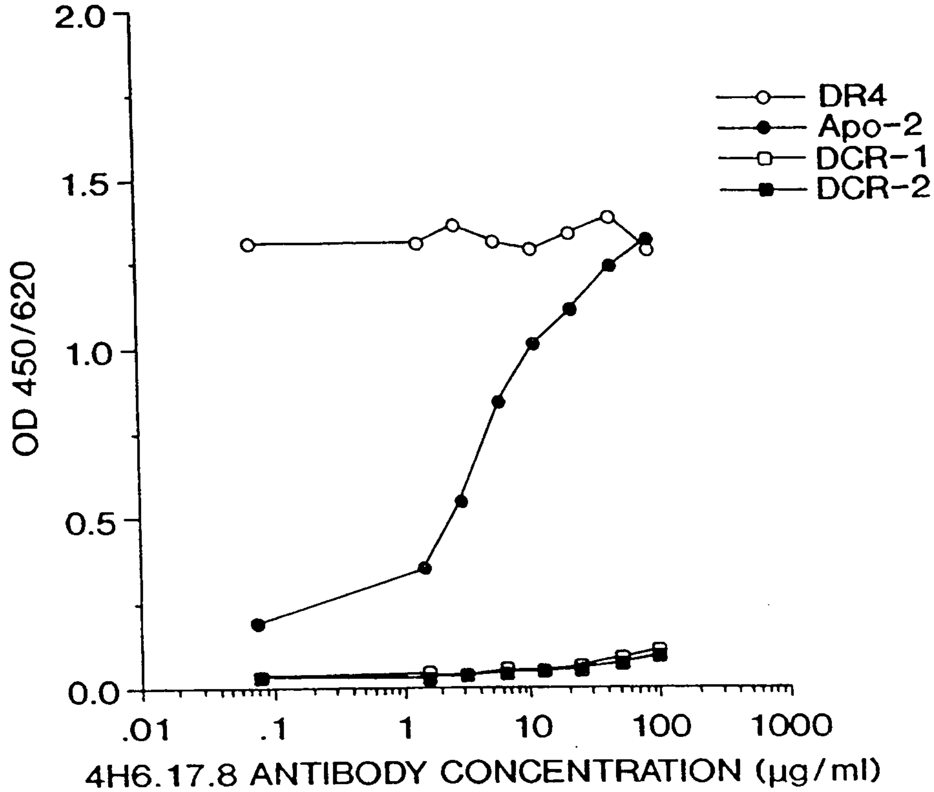

FIG. 6A

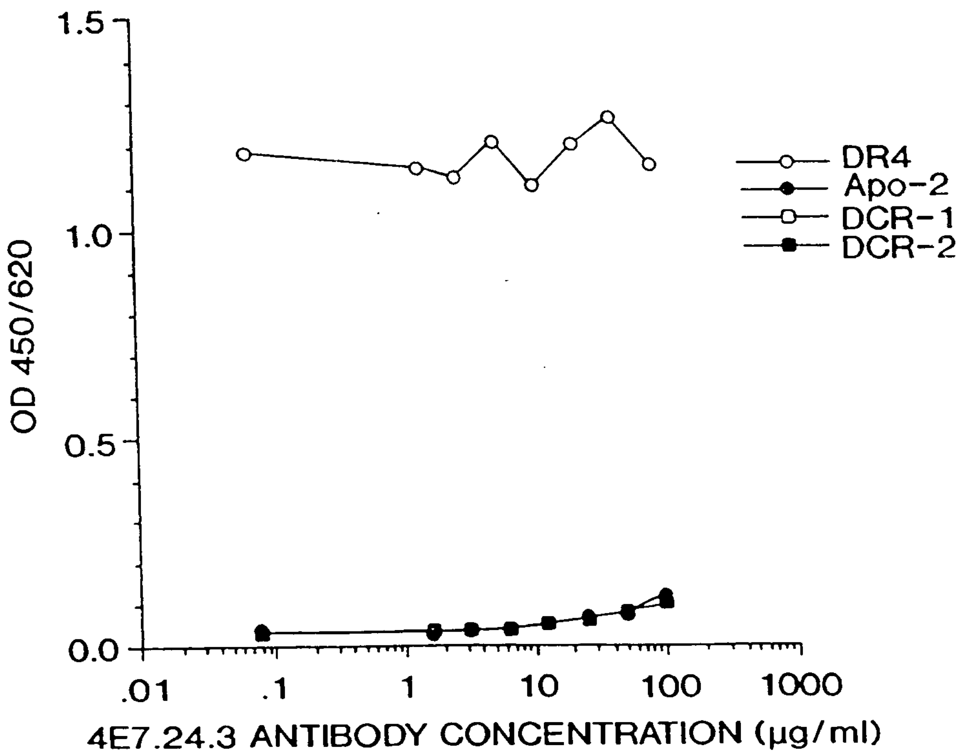

FIG. 6B

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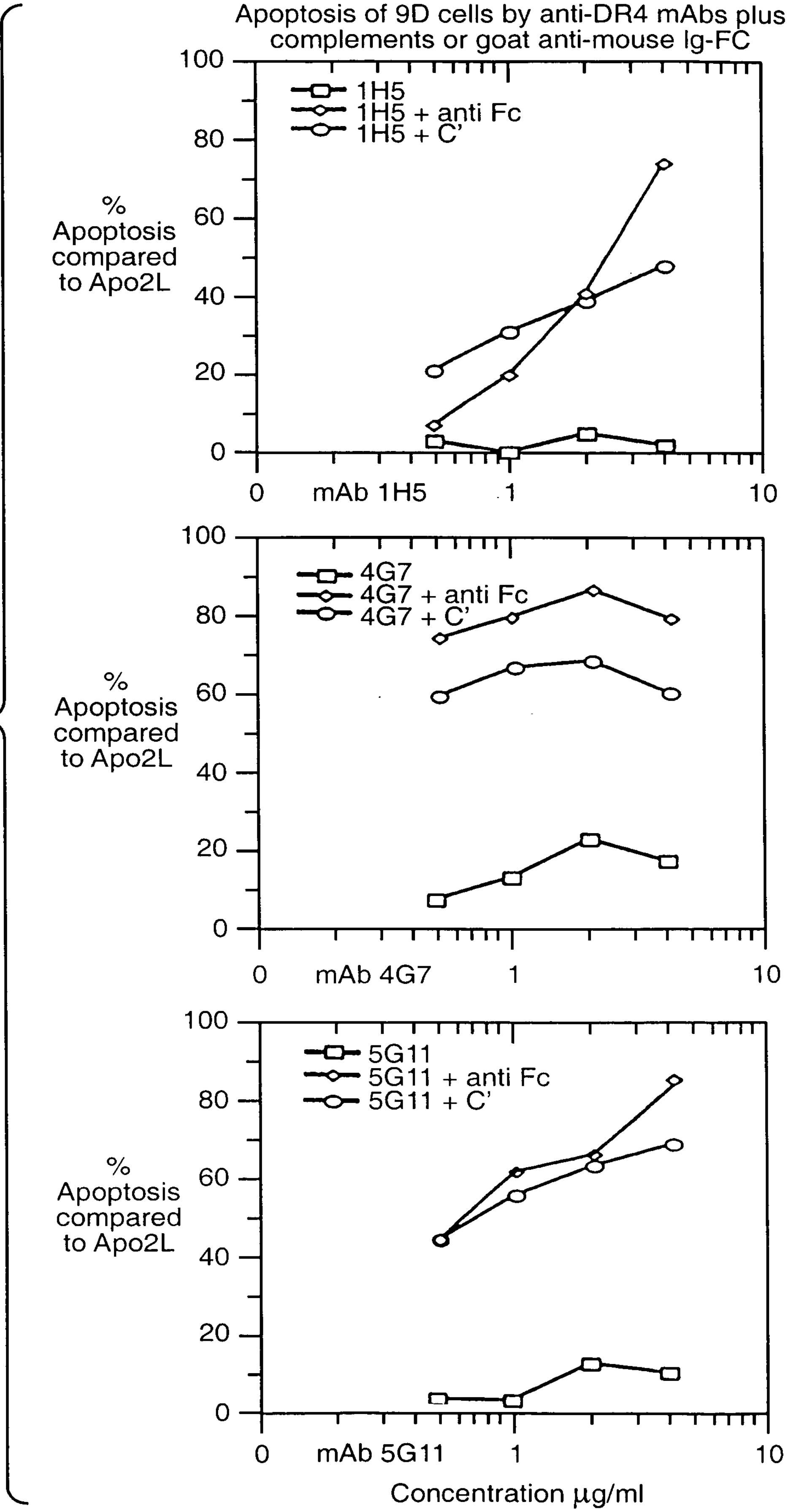
FIG._8A



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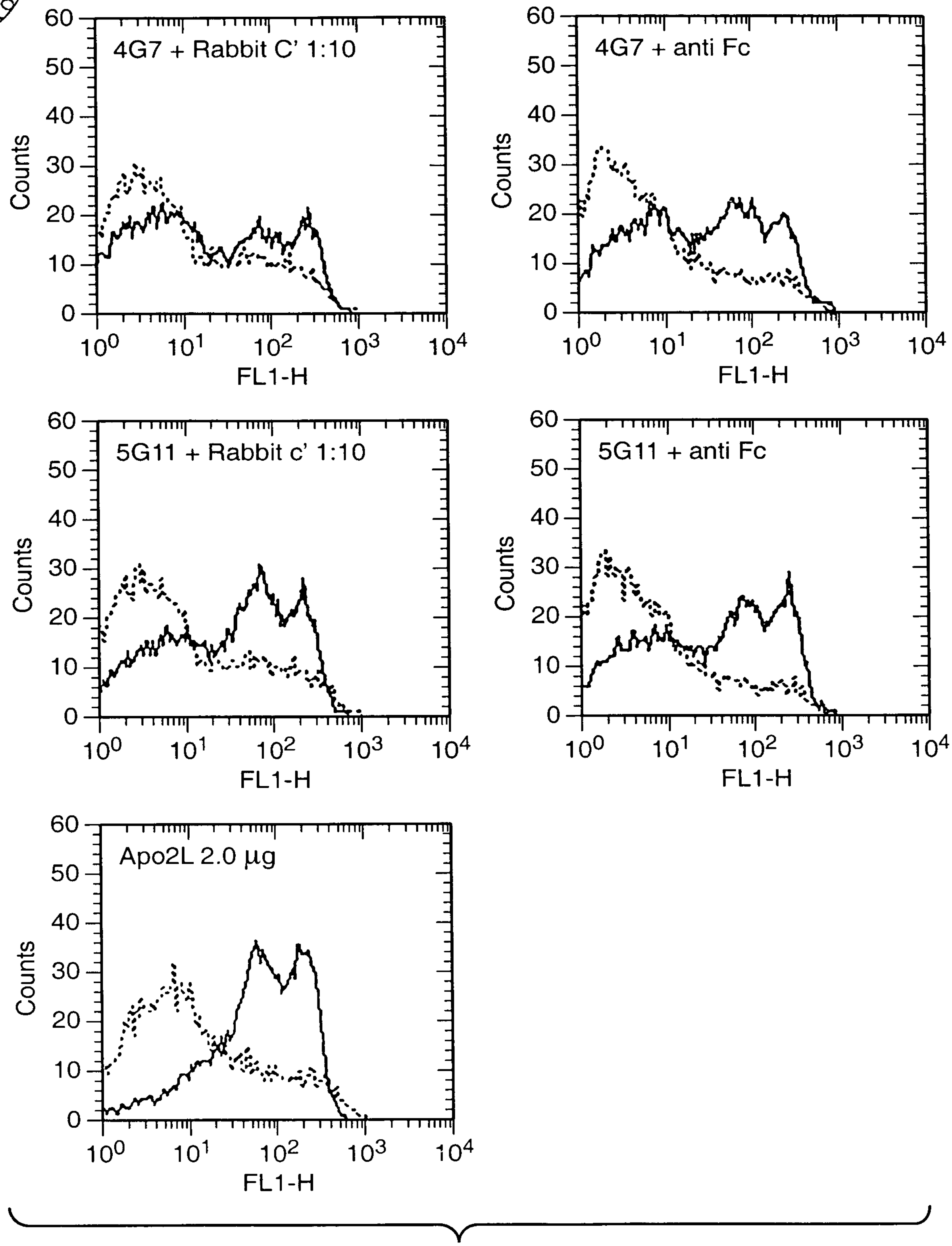

FIG._8B

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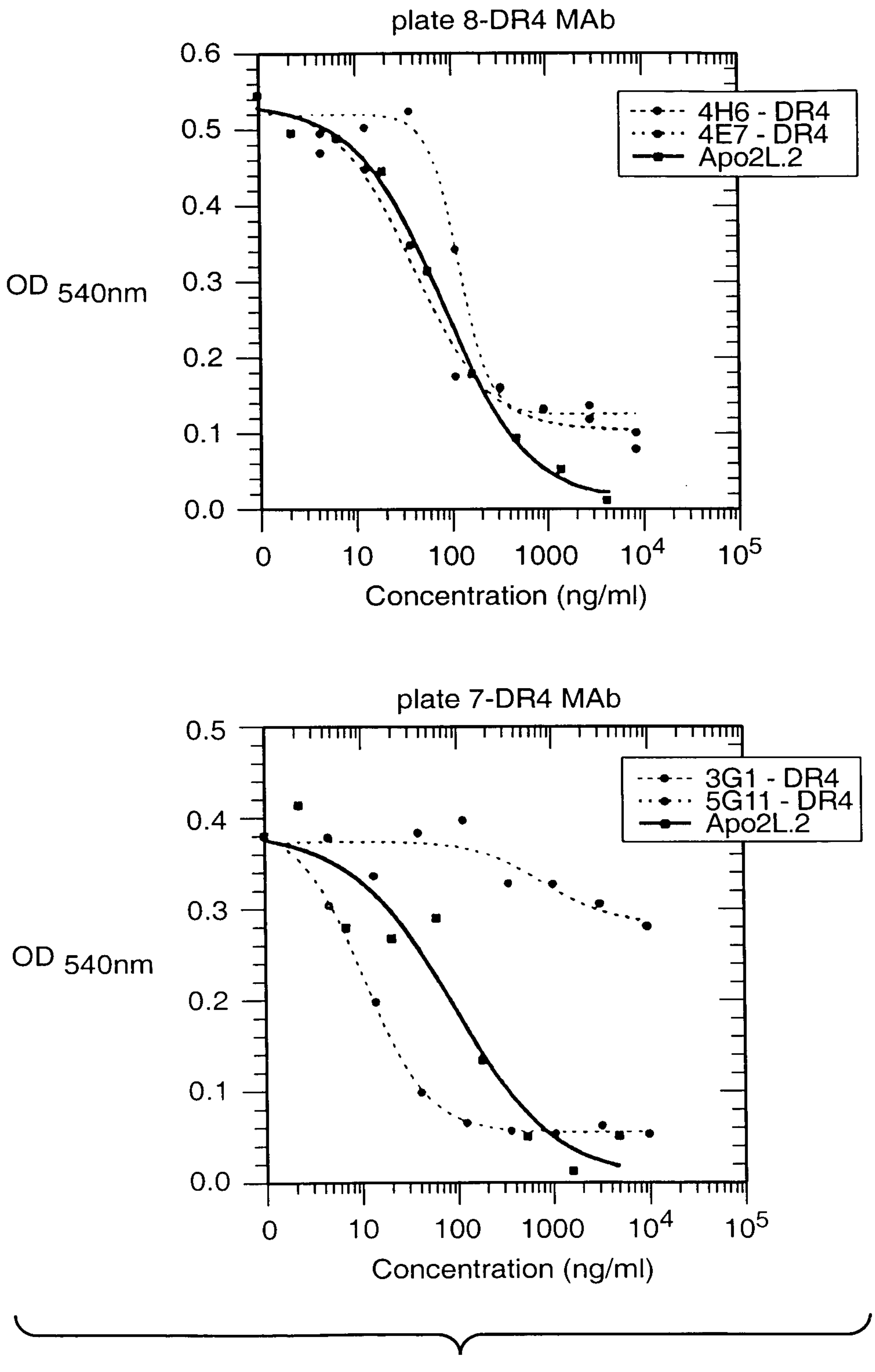

FIG._9A

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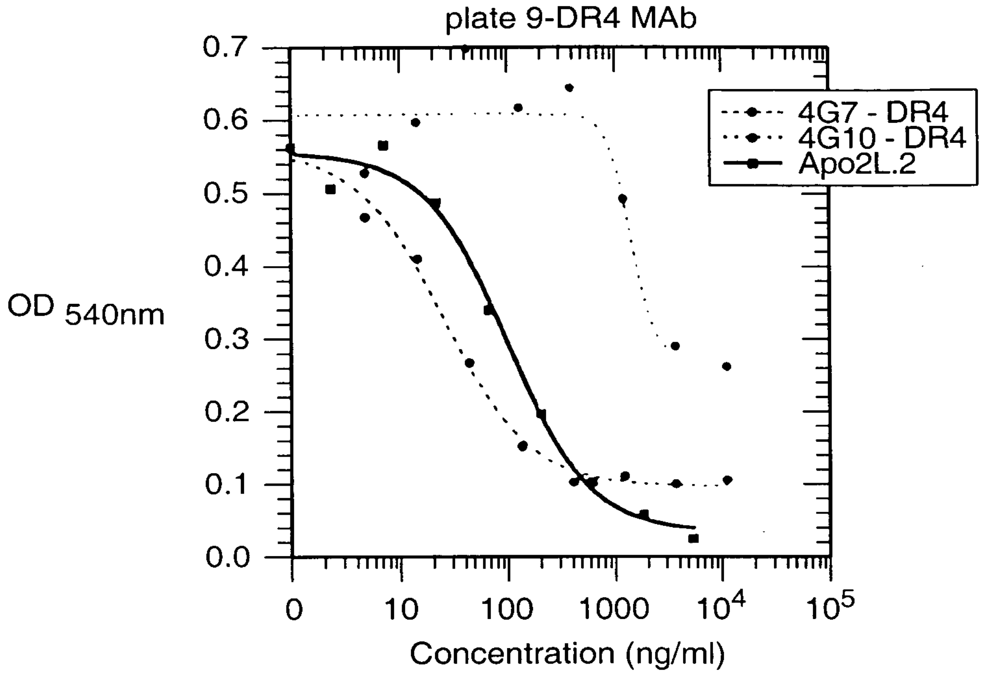

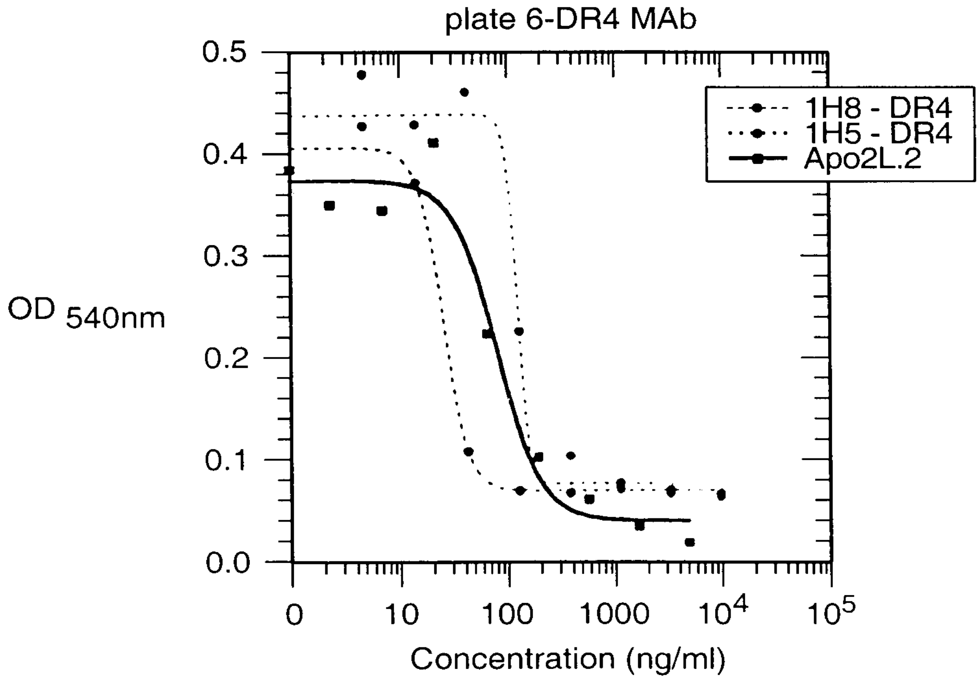

FIG._9B

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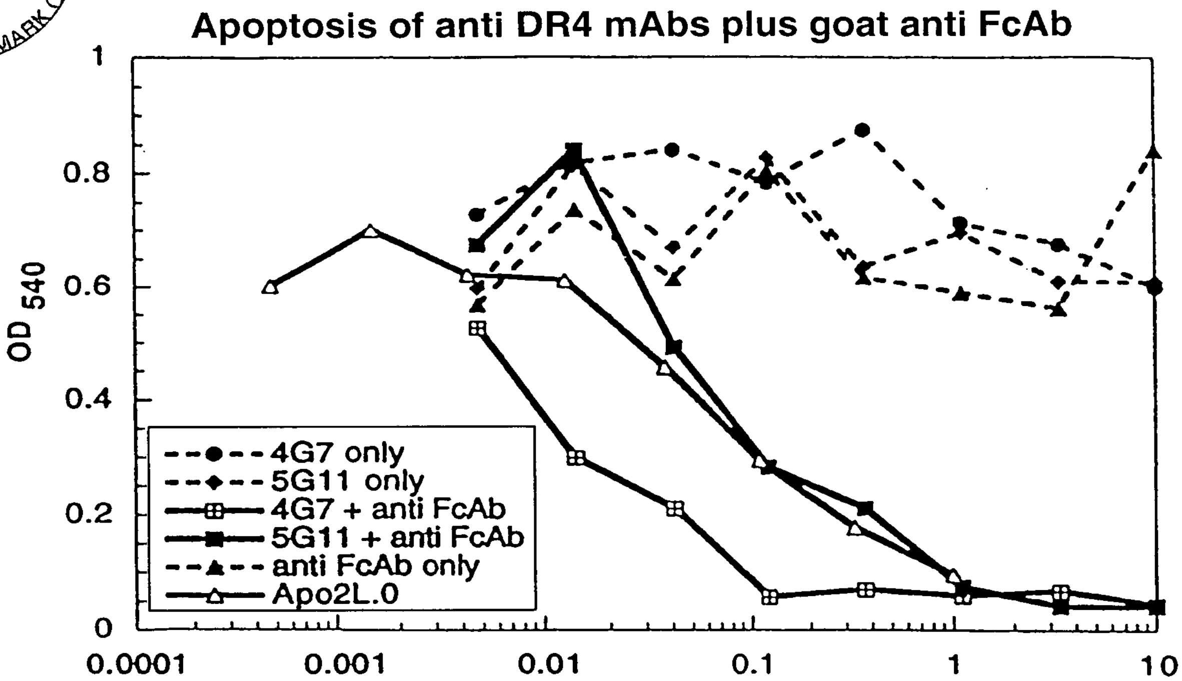

FIG._10A

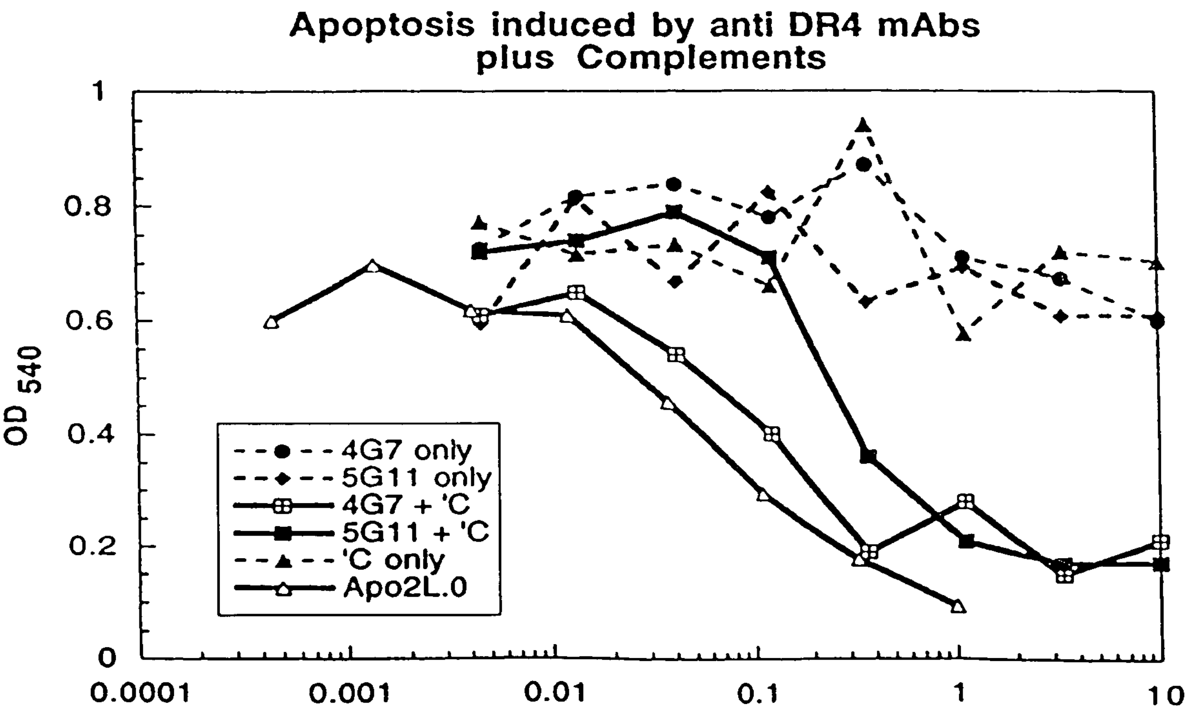

FIG._10B

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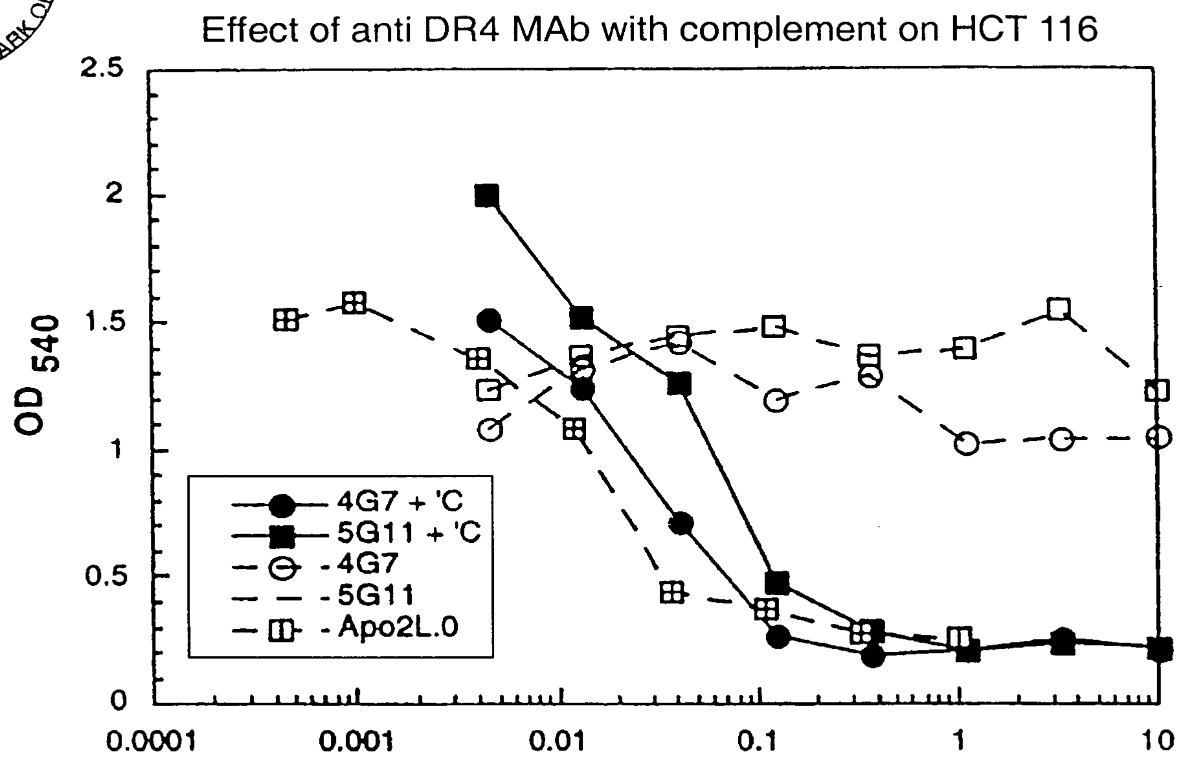

FIG._11A

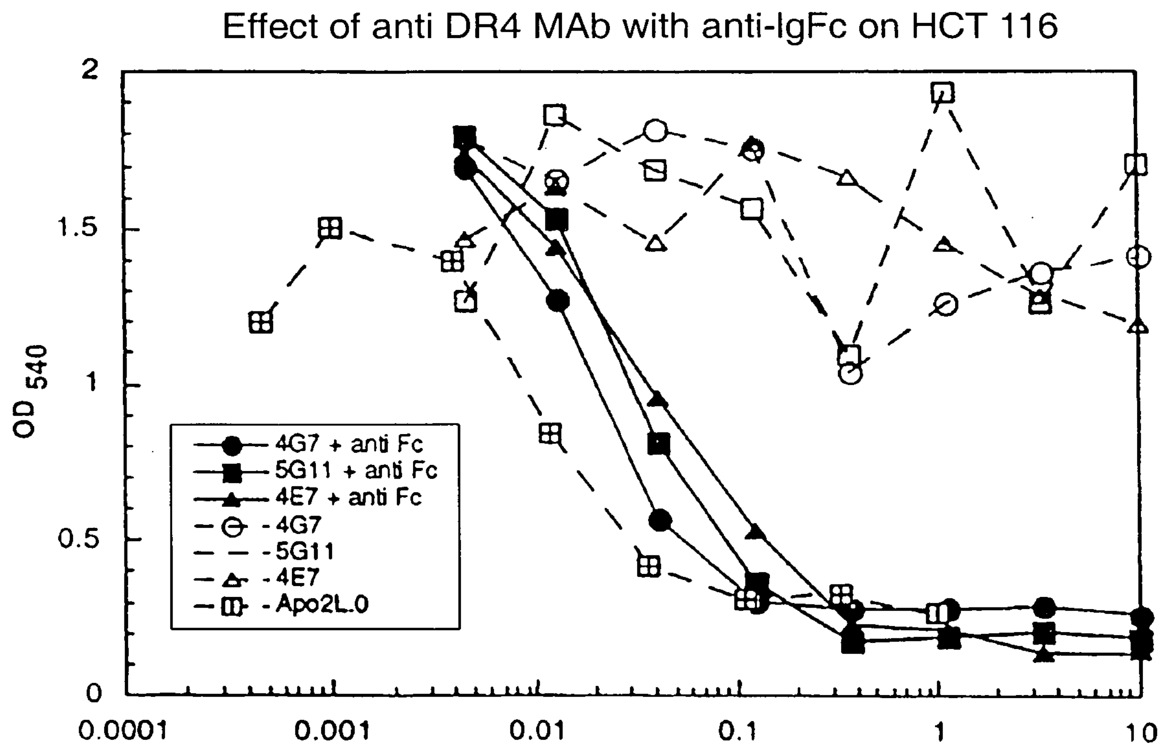

FIG._11B

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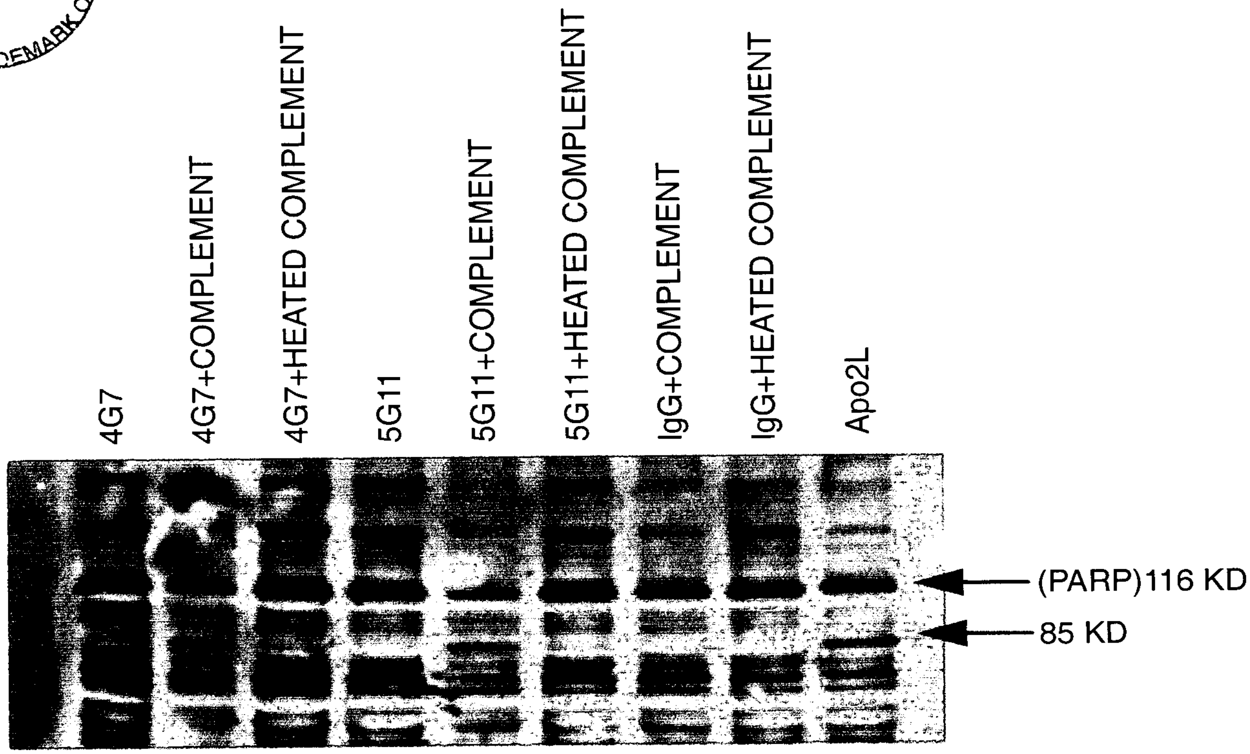

FIG._12

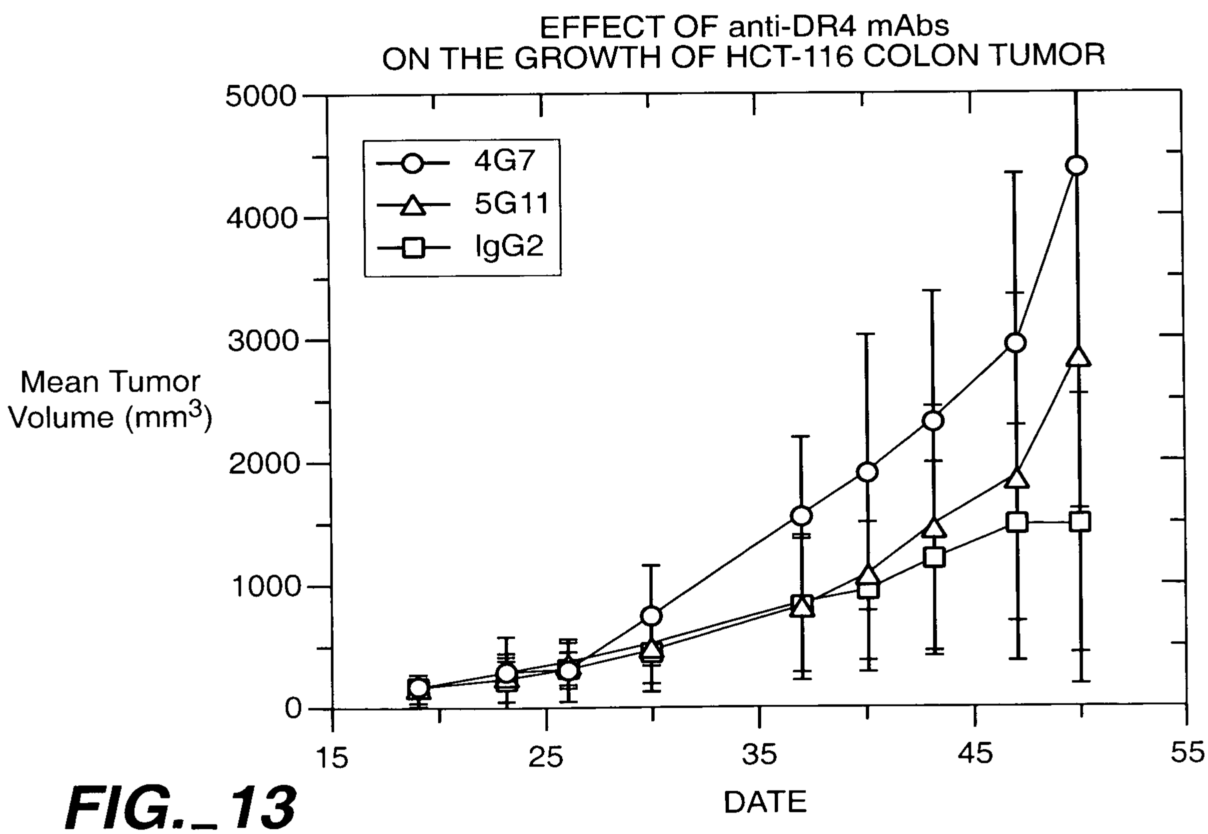

FIG._13

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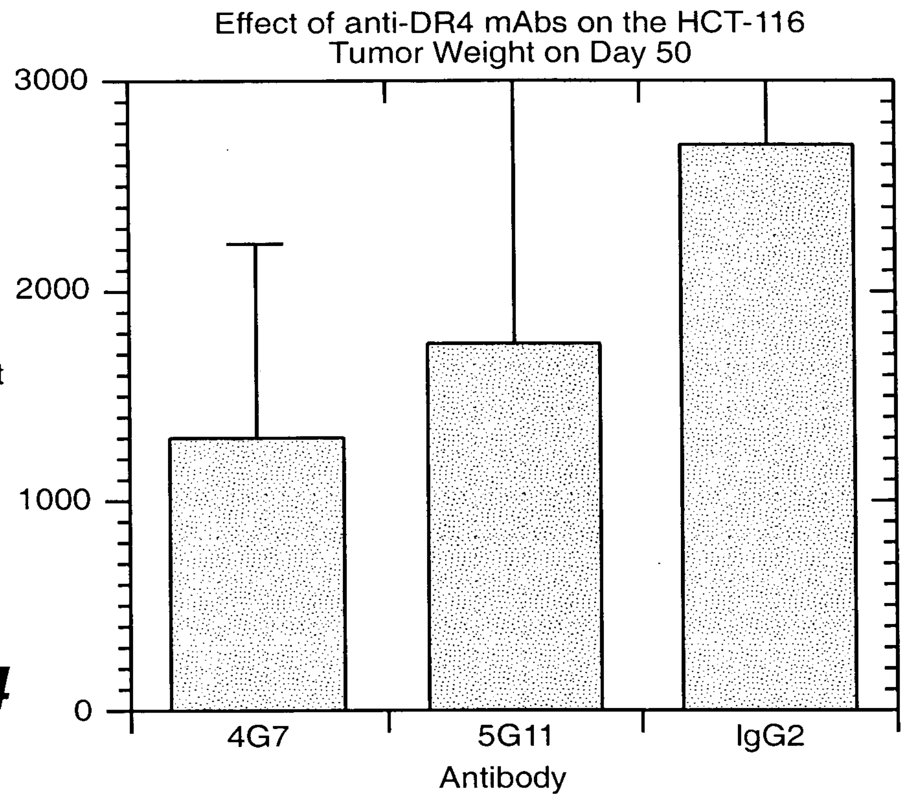

FIG._14

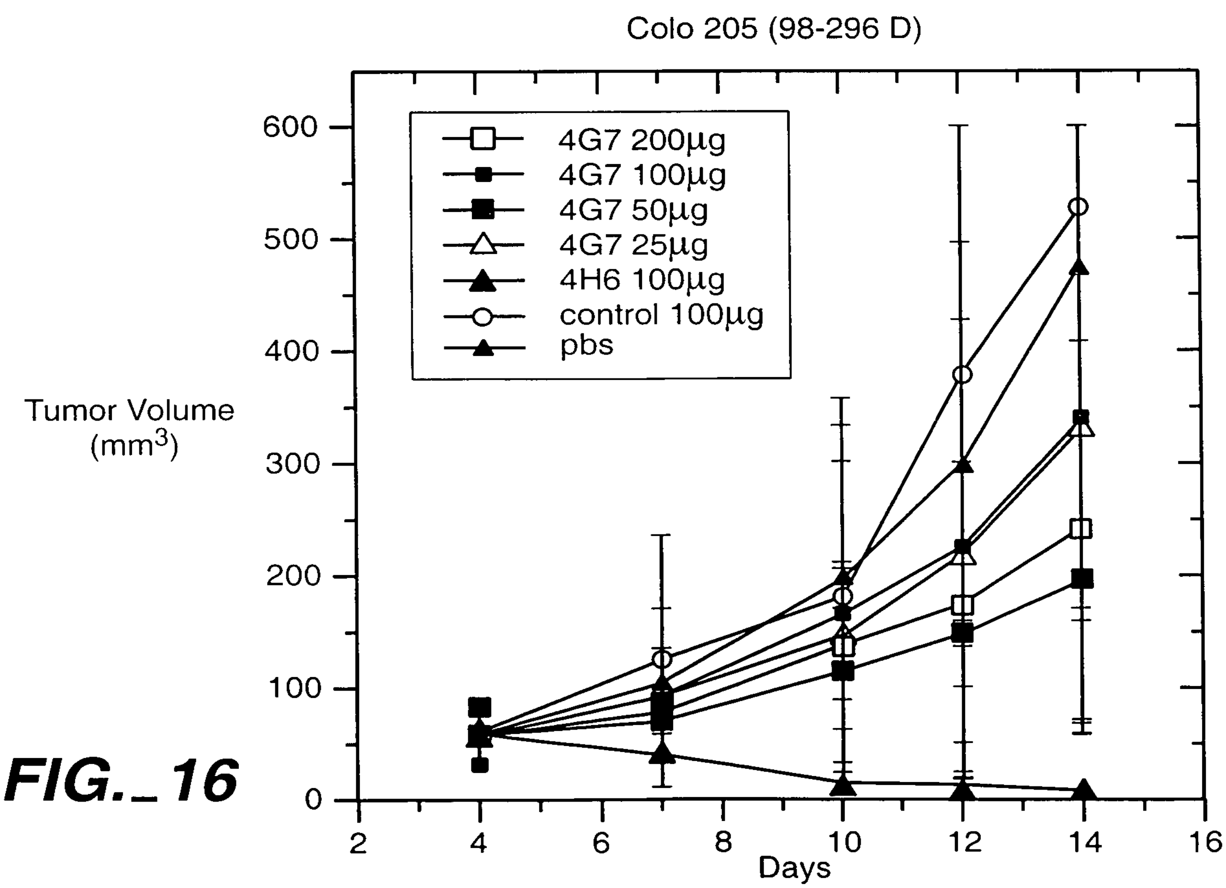

FIG._16

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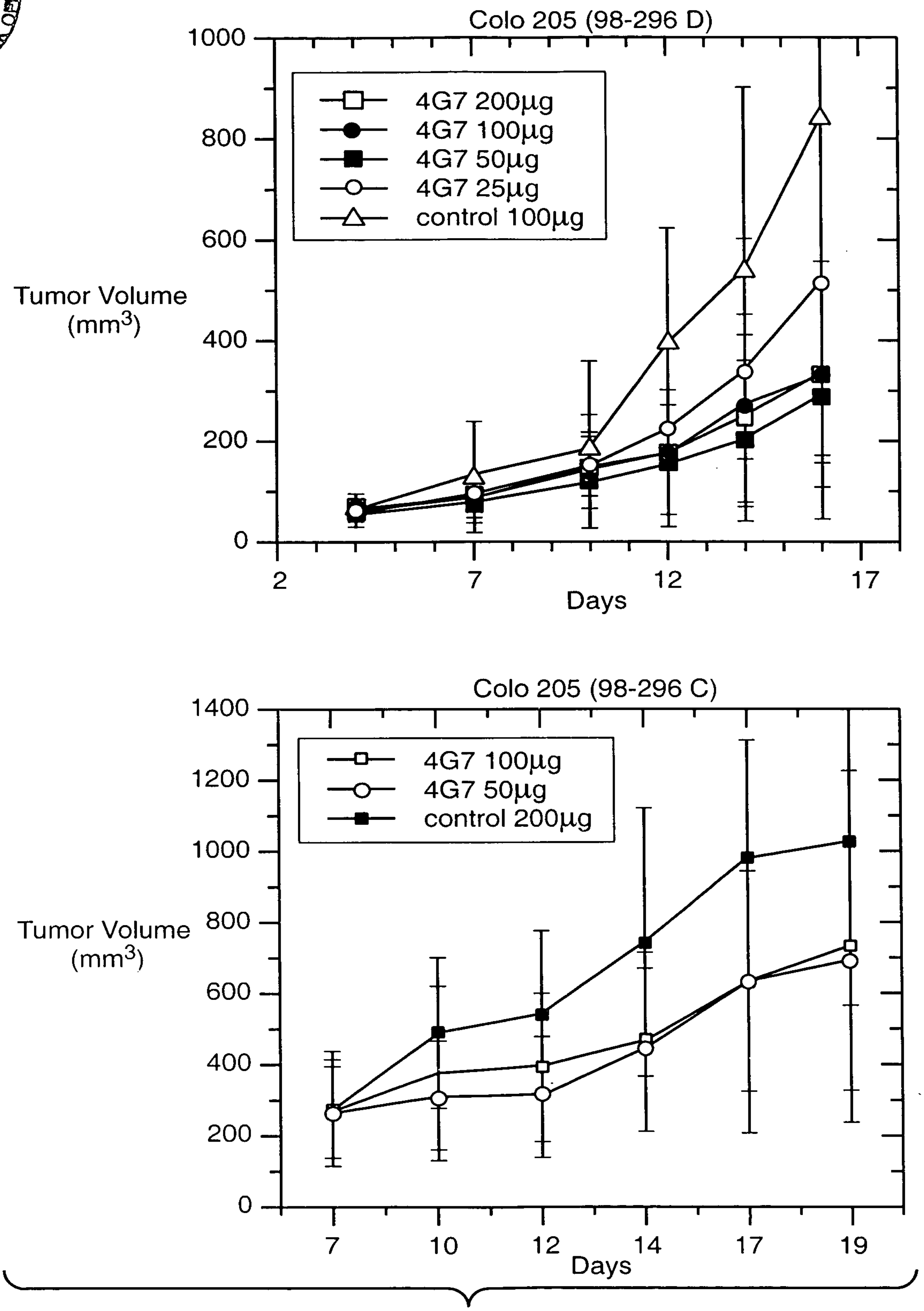

FIG._15

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GENERAL CHARACTERISTICS OF ANTI-DR4 mAbs

	Isotype	Kd-1 (pm)	Apop w / o L	Apop + &Fc	Apop + C'	Block	Cross Reactivity DR4	DR5	DCR1	DCR2
1H5.24.9	IgG2a			-	-	ND	+++	-	-	-
1H8.17.5	IgG1			+	ND	ND	+++	-	-	-
3G1.17.2	IgG1			-	ND	-	+++	-	-	-
4E7.24.3	IgG1	2	+ / -	+	-	-	+++	+	-	+ / -
4G7.18.8	IgG2a		+ / -	+	+	-	+++	-	-	-
4H6.17.8	IgG1	5	+ / -	+	-	+	+++	+	-	-
4G10.20.6	IgG1			+	ND	-	+++	+	-	-
5G11.17.1	IgG2b	22		+	+	ND	+++	++	-	-

All these mAbs recognize DR4 on 9D cells and immune precipitate DR4-IgG.

w / o L: The apoptotic ability of mAbs by themselves was detected on 9D cells, skmes cells, HCT116 and colo 205

+ &FC: The apoptotic ability of mAbs was determined in combination with goat anti-mouse IgG FC.

+ C': The apoptotic ability of mAbs was determined in the presence of rabbit complement

Degrees of binding (+) to DR5 by Mabs 4E7 and 4H6 at 10 μg / ml are 15% of the binding of DR4.

FIG._17